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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,845	10/15/2003	Michael T. Lotze	UPT-004	9535

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EXAMINER	
JUEDES, AMY E	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/688,845	LOTZE ET AL.	
	Examiner	Art Unit	
	Amy E. Juedes, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-29 and 31-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 11/20/06, are acknowledged.

Claim 27 has been amended.
Claims 28-35 have been added.
Claims 1-35 are pending.

2. Claims 1-26 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claim 30 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species.

Claims 27-29 and 31-35 are being acted upon.

3. The rejection of the claims under 35 U.S.C. 102 as being anticipated by U.S. Patent 6,017,527 is withdrawn in view of Applicant's amendment. The '527 patent does not teach a composition comprising IL-12 and an unloaded or unpulsed dendritic cell.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 27 stands rejected, and claims 28-29 and 31-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhardwaj et al., 1996, as evidenced by Hackstein et al., 2002.

As set forth previously, Bhardwaj et al. disclose a culture (i.e. a composition) comprising ex-vivo purified dendritic cells and IL-12 (see pg. 715 and Table 1 in particular). As evidenced by Hackstein et al., dendritic cells arise from CD34+ stem cells, and thus the ex-vivo isolated dendritic cells taught by Bhardwaj et al. are CD34+ derived. It is noted that the term "therapeutic composition" carries little patentable weight in the absence of evidence of a structural difference, since it refers to an intended use of the composition. The culture medium taught by Bhardwaj et al. (RPMI supplemented with gentamicin, human serum and HEPES buffer) is not incompatible with biological activity and therefore meets the limitations of a "therapeutic composition".

Applicant's arguments filed 11/20/06 have been fully considered, but they are not persuasive.

Applicant argues that Bhardwaj does not disclose a therapeutic composition, since the composition of Bhardwaj is a crude culture that contains impurities that would not be suitable for administration to a patient.

Cells in culture are considered to be compatible with physiological conditions and not incompatible with pharmaceutical use. Absent a limiting definition of "therapeutic composition", cells in culture are encompassed by the broadest reasonable definition of "therapeutic composition". In fact, the instant specification discloses on page 15 that the composition of the invention may be administered in any physiological solution. As noted above, the cell culture medium taught by Bhardwaj is compatible with physiological conditions, and thus meets the limitations of a "therapeutic" composition. It is noted that claims 32-33 have been included in the rejection, since the composition taught by Bhardwaj would inherently be effective for treating an infectious lesion or exhibit anti-tumor effects, since it is identical to the composition of the instant claims. Furthermore, claim 24 has been included since the culture medium taught by Bhardwaj comprises gentamicin (i.e. a small molecule).

6. Claim 27 stands rejected, and claims 28-29 and 31-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Kelleher et al., 1998.

As set forth previously, Kelleher et al. disclose a culture (i.e. a composition) comprising dendritic cells and IL-12 (see pg. 750 in particular). Kelleher et al. further teach that said dendritic cells are derived from CD34 bone marrow stem cells (see abstract and pg. 750 in particular). It is noted that the term "therapeutic composition" carries little patentable weight in the absence of evidence of a structural difference, since it refers to an intended use of the composition. The culture medium taught by Kelleher et al. (RPMI supplemented with penicillin, streptomycin, glutamine, FCS, and 2 mercaptoethanol) is not incompatible with biological activity and therefore meets the limitations of a "therapeutic composition".

Applicant's arguments filed 11/20/06 have been fully considered, but they are not persuasive.

Applicant argues that Kelleher does not disclose a therapeutic composition, since the composition of Kelleher is a

crude culture that contains impurities that would not be suitable for administration to a patient.

Cells in culture are considered to be compatible with physiological conditions and not incompatible with pharmaceutical use. Absent a limiting definition of "therapeutic composition", cells in culture are encompassed by the broadest reasonable definition of "therapeutic composition". In fact, the instant specification discloses on page 15 that the composition of the invention may be administered in any physiological solution. Furthermore, the instant specification discloses on page 15 that the composition of the invention may be administered in any physiological solution. As noted above, the cell culture medium taught by Kelleher is compatible with physiological conditions, and thus meets the limitations of a "therapeutic" composition. It is noted that claims 32-33 have been included in the rejection, since the composition taught by Kelleher would inherently be effective for treating an infectious lesion or exhibit anti-tumor effects, since it is identical to the composition of the instant claims. Furthermore, claim 24 has been included since the culture medium taught by Kelleher comprises penicillin (i.e. a small molecule).

7. The following are new grounds of rejection necessitated by Applicant's amendment.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 28 is indefinite in the recitation of antigen "present" cell. The claim is unclear since it is grammatically incorrect.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out

his invention.

Claim 34 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is insufficient written description to demonstrate that applicant was in possession of the claimed genus of agents comprising "proteins", "peptides", "small molecules", "antibodies", "antibody fragments", and "lipids".

The instant claim might encompass a broad range of structurally and functionally different agents. For example, the claim might encompass virtually any protein, antibody, small molecule, or lipid. The specification does not describe any structural or functional characteristics that said agents are required to possess. Furthermore, the only species disclosed by the instant specification are IL-12 and G-CSF. The disclosure of two closely related protein cytokines is not sufficiently representative of the virtually unlimited number of structurally and functionally different agents encompassed by the claim. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

10. Claims 32-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed composition would function to treat infectious lesions, or exhibit anti-tumor effects, as broadly claimed.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of

predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The instant claims are drawn to a composition comprising an antigen presenting cell and immunostimulatory cytokine that is effective for treating infectious lesions, and exhibits anti-tumor effects. However, claim 31 recites that the "immunostimulatory" cytokine can be TGF-β. Thus, the claims encompass a composition comprising TGF-β that is effective for treating tumors or infectious lesions. However, TGF-β is an immune suppressive cytokine that can induce progression of tumors (see Miyazono et al. page 230 and 233 in particular). Furthermore, the instant claims encompass a composition effective against tumors or infectious lesions that comprise antigen presenting cells that have not been pulsed with antigen. While there is some evidence that antigen-unpulsed dendritic cells expressing certain cytokines (e.g. IL-12) are effective for treating tumors (see Furumoto et al., 2000), therapy of infectious disease is usually performed with antigen pulsed dendritic cells to induce a specific immune response against the infection. In fact, Ramirez-Pineda et al. demonstrate that treating lesions associated with leishmania requires dendritic

cells to be pulsed with specific antigen, and antigen unpulsed dendritic cells are ineffective in treating the lesions (see Fig. 1 in particular).

Thus, given the state of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims. However, the only examples provided by the instant specification demonstrate that a composition comprising IL-18 and dendritic cells is effective in treating tumors in an animal model. This is not commensurate in scope with the instant claims, which encompass a composition for treating tumors, or any infectious lesion, comprising any immunostimulatory cytokine, including TGF-β. Accordingly, it would require undue experimentation to use the composition, as broadly claimed, for treating infectious lesions or tumors.

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the

organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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1/26/07
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